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PANCREATIC CANCER CLUSTER INVESTIGATION OF LIVINGSTON AND PARK COUNTY, MONTANA

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AND
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ABSTRACT

A putative cluster of pancreatic cancer cases in Park County, Montana, from 1980 through 1989 was investigated by the Montana Department of Health and Environmental Sciences and Agency for Toxic Substances and Disease Registry (ATSDR) through review of death certificates and medical records. The observed number of white-male pancreatic cancer deaths for Livingston, the largest community in Park County, Montana, from 1980 through 1989 was found to be elevated when compared to the age-adjusted number of deaths expected on the basis of 1980 through 1988 U.S. age-and-sex-specific pancreatic cancer mortality rates and the 1980 census age and sex distribution for Livingston. Based on the information obtained in this investigation, smoking did not appear to be responsible for this increase. An apparent clustering of cases among people who worked in the railroad industry may have reflected occupational patterns in the community as a whole or indicated the presence of a risk factor. Also, addresses of decedents did appear to cluster along the railroad right-of-way, but further investigation would be required to determine whether this pattern is unusual, given the age of the decedents at the time of death. ATSDR recommends that a further investigation be conducted on this apparent cluster of pancreatic cancer cases in Livingston, Montana.

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PANCREATIC CANCER CLUSTER INVESTIGATION OF LIVINGSTON AND PARK COUNTY, MONTANA

INTRODUCTION

Livingston and other Park County, Montana, residents potentially exposed in the past to groundwater and airborne toxicants requested assistance from the Montana Department of Health and Environmental Sciences (MDHES) and the Agency for Toxic Substances and Disease Registry (ATSDR). MDHES requested technical assistance from ATSDR in identifying available options for health investigations or studies of residents of Park County, including Livingston.

Initially, MDHES provided ATSDR with cancer mortality statistics for the period 1986 through 1988 for Park County, Montana, from the Montana Cancer Registry. MDHES requested assistance in the review of the mortality statistics to determine whether there was an increase in digestive tract cancer mortality over background levels for those years. As a result, the Division of Health Studies of ATSDR undertook a preliminary investigation of cancer mortality in Park County.

Objectives

This study was undertaken to:

(1) Determine the numbers of cases of pancreatic cancer from 1980 through 1989 in Livingston, in Park County exclusive of Livingston, and in Park County as a whole and to compare these numbers with the expected numbers of pancreatic cancer cases based on U.S. pancreatic cancer mortality for the same period.

(2) Determine whether any association with residential location, occupational history, smoking, or type of pancreatic cancer was suggested by the information available.

(3) Determine whether further evaluation was indicated.

BACKGROUND

History

The Northern Pacific Railroad and the Burlington Northern Railroad previously operated a railroad repair and fueling station in Livingston, Montana. Environmental sampling conducted since 1985 has revealed widespread contamination of groundwater and soil by several toxicants including diesel fuel and chlorinated volatile organic solvents (primarily degreasers) (Figures 1 and 2). Analyses of samples from monitored

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Livingston city wells revealed trace levels of these toxicants. Other known sources of potential toxicant exposures included two sawdust burners (which no longer operate) in the southwestern and northeastern areas of the city and coal-burning locomotives generating smoke prior to the mid-1950's.

The Northern Pacific Railroad's main line, which subsequently became the southern line of the Burlington Northern Railroad, runs through the town of Livingston along Park Street (Figure 3). Montana officials and Park County residents have indicated that former railroad activities included routine idling of trains on the tracks in the center of Livingston to fire up (that is, bring to an operating condition from a cold or idle start) their engines. Under these circumstances, trains expelled large quantities of smoke and fumes on a daily basis for decades. This anecdotal information suggested a potentially high magnitude of airborne exposure to toxicants in the past. However, the information was insufficient to quantify exposure magnitude or duration.

Characterization of the Site Prior to Study

Generally, prevailing winds in Livingston are from the southwest to the northeast; however, winds blow east intermittently, often for days at a time. Additional information about patterns of airborne dispersion in Livingston was obtained because MDHES was concerned about a large asbestos-contaminated waste pile at the Livingston railroad yard and monitored asbestos dispersion. (This information is cited with respect to the distribution of toxicants; asbestos exposure is associated with several types of cancer, but not with pancreatic cancer.) This monitoring showed that toxicants were often carried in appreciable concentrations counter to, as well as in, the prevailing wind direction, suggesting that airborne toxicant distribution was not a simple function of prevailing wind direction in Livingston.

Environmental data since 1985 have demonstrated soil contamination with volatile organic hydrocarbons in the area of the railroad yard and groundwater plumes of diesel fuel, dichloroethylene, trichloroethylene, and perchloroethylene extending into the area between Park Street and the Yellowstone River and northeast of Main Street (Figures 1 and 2). Currently, data for air, surface water, and food chain entities are limited or unavailable; however, the planned ATSDR Health Assessment and ongoing site investigations will better define contamination of these media.

Initial Review of Health Statistics

MDHES provided ATSDR with numbers of cancer deaths and rates for Montana, for Park County, and for Montana exclusive of Park County, for the period 1986 through 1988. MDHES classified these data into six diagnostic categories (Table 1), and presented ATSDR with a copy of the results of a statistical analysis that suggested an increased rate of malignant neoplasms of digestive organs and peritoneum in Park County, Montana, during the period 1986 through 1988 (Sperry, 1990).

Cancer mortality statistics for the five digestive tract cancer sites were listed by The International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9-CM) codes in a contingency table. Expected numbers of Montana cases in Park County and observed-to-expected (O:E) ratios were calculated (Table 2). The O:E ratio exceeded 2:1 for ICD-9-CM Code 156 (gallbladder cancer) and 157 (pancreatic cancer). Only two ICD-9-CM Code 156 cases were identified, and could have occurred by chance even if statistical methods indicated significance. The total number of ICD-9-CM Code 157 (pancreatic cancer) cases was seven, thus further investigation was deemed warranted for the pancreatic cancer cases. Broadening the study scope to include other types of cancers previously associated with exposures likely for Livingston residents (on the basis of available environmental toxicant data) or to include ICD-9-CM Code 156 cases was deemed unlikely to improve the chances of finding an association and might, depending upon the approach, dilute any association which might exist between residence or occupation and pancreatic cancer.

Pancreatic Cancer

Pancreatic cancer is an "insidiously developing, relentlessly progressive, and nearly universally fatal malignancy" (Cello, 1989). Death occurs in over 95 percent of the cases (Mayer, 1991). Crude incidence has increased significantly in the United States with the increase in the median life expectancy of the U.S. population (Mayer, 1991). In 1989, pancreatic cancer was the fourth most common cause of cancer-related mortality in men and the fifth most common in women (Kato et al, 1985). The male-to-female ratio appears to be 2:1 in most patient series (Cello, 1989). Pancreatic cancer rarely occurs before age 25, and the mean age at which it occurs is in the seventh and eighth decades of life (Cello, 1989). Occasionally, patients with pancreatic cancer manifest the signs and symptoms of chronic pancreatic diseases, such as chronic pancreatitis (Cello, 1989). However, no etiologic relationship has been established between acute or chronic pancreatitis and subsequent development of cancer of the pancreas (Mayer, 1991). Pancreatic cancer appears to be more common in blacks than in whites (Mayer, 1991). There were no nonwhite cases included in this study; the population of Park County is virtually all white (National Center for Health Statistics (NCHS), 1991).

Cigarette smoking is the most consistently observed risk factor for pancreatic cancer. Men who smoke more than 1 1/2 packs of cigarettes per day have a threefold increase in risk and women who smoke more than 1 pack per day have a twofold increase in risk compared with nonsmokers (Wynder et al, 1983). It is not clear whether the apparent association between cigarette smoking and pancreatic cancer represents direct carcinogenesis of cigarette smoke metabolites or an undefined exposure that occurs more frequently in smokers (Mayer, 1991).

Kato et al (1985) reported a strong positive association between residence in higher latitudes and pancreatic cancer incidence and a strong negative association with average ambient temperature. Pickle and Gottlieb (1980) reported an association between a large pancreatic cancer cluster in Louisiana and oil refining and paper manufacturing. No convincing data link pancreatic cancer to risk factors such as alcohol abuse, a history of diabetes mellitus, cholelithiasis, or coffee consumption (Mayer, 1991).

METHODS

Rationale for Study Design

Preliminary analysis of statistical information suggested an increased rate of pancreatic cancer mortality in Park County during the period 1986 through 1988. As a result, investigators decided to: (1) review the available medical records of all people who died of pancreatic cancer in Park County from 1980 through 1989; (2) obtain information on the population distribution by age and sex in Park County and Livingston, Park County's largest community, during this time period; and (3) obtain U.S. pancreatic cancer mortality data and the U.S. population distribution by age and sex for the period cited. This information would allow investigators to: (1) confirm the accuracy of the diagnoses; (2) determine the observed and expected numbers of pancreatic cancer deaths in Park County, in Livingston, and in Park County exclusive of Livingston; (3) calculate pancreatic cancer death rates for Park County, Livingston, and Park County exclusive of Livingston and adjust the rates to the age distribution of the U.S. population; and (4) obtain available information on additional factors such as smoking, occupation, age at death, and residence. Information on smoking, occupation, age at death, and residence is useful in ensuring that any observed excess of pancreatic cancer mortality is not a result of the age distribution of the population and in exploring possible associations with environmental factors.

Case Definition

The case definition for this phase of study was any resident of Park County, Montana, who died during the period January 1, 1980, through December 31, 1989, whose death certificate was coded by nosologists as ICD-8 or ICD-9-CM Code 157. (ICD-8 and ICD-9-CM codes are identical for pancreatic cancer.)

Medical Records Review

Using the address listed on each death certificate, investigators obtained copies of death certificates for persons who had resided in the study area at the time of their death. All were individuals who had died of pancreatic cancer in Park County during the years 1980 through 1989 and who were listed by the Montana Cancer Registry. Medical records librarians at the Livingston Memorial Hospital directed our attention to additional cases of Park County residents who died of pancreatic cancer. The investigators contacted the hospitals listed on the death certificates and reviewed the medical records of the decedents. Each medical record was read in its entirety, and a medical records abstraction form was completed (Appendix) using the following variables:

(1) Local file and hospital record number;
(2) Age, date of birth, sex, and race of each subject;

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(3) Procedures used to diagnose pancreatic cancer;
(4) Residential address of each subject;
(5) Length of residence of each subject at each indicated address (when available);
(6) History of diabetes mellitus;
(7) History of smoking;
(8) History of alcohol use;
(9) Medications used (at the time of death and, as much as possible, historically);
(10) Pertinent dietary history;
(11) History of other diseases;
(12) Occupational history; and
(13) Spousal occupational history.

Data Analysis Methods

The observed male, female, and total numbers of cases were tabulated for residents of the study area according to which of the following categories best described the mailing address: (1) Livingston (zip code 59047), and (2) Park County exclusive of Livingston. (The observed numbers of cases meeting the case definition for this study were tabulated and were not modified by assessment of the quality of the diagnostic evaluation.) Expected numbers of pancreatic cancer deaths among white male and female residents were calculated using the pancreatic cancer death rates (ICD-9-CM Code 157) for the period 1980 through 1988 obtained from NCHS (1988) (rates were not available for 1989) and the resident population breakdown by sex and 5-year age groups for the three areas (U.S. Bureau of the Census, 1980). The probabilities (p-values) of at least the number of cases observed in the the two address categories and Park County as a whole occurring by chance alone were calculated using a Poisson distribution.

The Bonferroni method was used to correct for the fact that the study hypothesis was tested with the same data set that was used to generate the hypothesis. The Bonferroni method requires that the chosen p-value (conventionally 0.05) be divided by the the number of comparisons made (Bailar and Mosteller, 1986). Since the data set originally used to generate the hypothesis that there was an excess of pancreatic cancer listed five digestive-tract cancer sites, the p-value used in this case was 0.01. Sex-specific, age-adjusted pancreatic cancer death rates were also calculated for the three areas and compared with the 1985 sex-specific rates (NCHS, 1988).

The information obtained from the review of the medical records on smoking history, occupational history, and residential location was tabulated for comparison between men and women in Livingston and in Park County exclusive of Livingston. People were classified as smokers if they had: (1) a history of smoking noted in their medical records, or (2) a history of having quit smoking within 25 years prior to hospital admission. People were classified as nonsmokers if they: (1) were identified as nonsmokers in their medical records, or (2) had a history of having quit smoking more than 25 years prior to hospital admission. Cases with no smoking history given were counted as unknown.

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NCHS (1990) revealed that crude and age-adjusted U.S. percentages of smokers were available for 1965, 1974, 1979, 1983, 1985, and 1987, and ranged from 31.0 to 51.6 percent for males and from 26.5 to 34.0 percent for females (Table 3). The critical time period for development of the observed pancreatic cancers is probably best represented by the 1965 percentages. Therefore, this percentage (52%) was used to calculate the maximum increases that should have occurred in study area pancreatic cancer death rates over U.S. rates for a worst possible case in which the percentage of smokers among the Livingston male cases (60 percent) was assumed to apply to the entire Livingston population (Figure 4). Furthermore, in the absence of quantitative information concerning the smoking habits of all the decedents, the threefold increase in risk noted by Wynder (1983) for males smoking 1 to 1 1/2 packs of cigarettes per day was assumed by the investigators to apply to all smokers.

Available residential locations of decedents were plotted on a street map of Livingston (Figure 3). This plot was used to determine whether a spatial relation to possible environmental exposure sources could be observed.

RESULTS

Medical Records Review

The death certificates indicated that decedents expired at: (1)Livingston Memorial Hospital, Livingston, Montana; (2) Ft. Harrison Veterans Administration Hospital, Helena, Montana; (3) Bozeman Deaconess Hospital, Bozeman, Montana; (4) Billings Deaconess Hospital, Billings, Montana; or (5) home. Medical records were located for all but the two people who died at home. Livingston Memorial Hospital also provided copies of medical records from three additional fatal cases of pancreatic cancer not found in the initial search of the Montana Cancer Registry and for which death certificates could not initially be obtained from the state. Of the five people for whom medical records were not available or death certificates initially located, three met the case definition.

Of the 23 people indicated by death certificate or medical record to have died of pancreatic cancer, a total of 20 met the case definition (Figure 5). Of these 20, 14 had Livingston addresses and 6 had Park County addresses outside of Livingston. (The three additional people whose records were provided by Livingston Memorial Hospital were two women who resided in Livingston and one man who resided in Park County exclusive of Livingston.) To the extent ascertainable from the medical records, none of the 20 decedents were members of the same family.

Although collected on the medical records abstraction form, four variables--history of diabetes mellitus, alcohol use, medication use, and dietary habits--were not included in the analysis because review of the literature on pancreatic cancer indicated no valid associations with these factors. The medical records did not provide adequate information to consider length of residence or spousal occupation in the analysis.

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Characteristics of Livingston Cases

Of the 14 people with Livingston addresses, 11 were men and 3 were women. Categories of diagnostic criteria included clinical presentation (including presenting symptoms and signs) in eight cases, including exploratory laparotomy in seven cases and abdominal ultrasound or computerized axial tomographic (CT) scan in seven cases. (In some cases, more than one of these categories of diagnostic criteria were employed.) Four of the remaining six were histologically confirmed as adenocarcinoma and one as an islet cell pancreatic cancer. The sixth of the remaining cases expired at home; no medical record or further information was available. Four of the male and one of the female cases had a history of a diagnosis or "probable" diagnosis of another type of cancer in addition to pancreatic cancer (Table 4).

Of the eight cases diagnosed by clinical presentation and not tissue examination, six lacked biopsy evidence of malignancy either because no biopsy was taken during exploratory laparotomy or because the biopsy tissue did not reveal malignant cells. However, in all six cases, a strong diagnostic impression of pancreatic cancer was reported because of the location and pattern of extension of the pancreatic mass and other features of the clinical presentation. In the seventh case, an abdominal CT scan revealed a pancreatic tail mass and metastases in the liver. The patient was cachectic and died before further diagnostic evaluation could be performed. In the eighth case, the diagnosis of pancreatic cancer was questioned by the physician writing the final discharge summary.

Information on Possible Risk Factors for Livingston Cases

Of the 11 male cases in Livingston, 6 were counted as smokers; 1 did not have any smoking history indicated in the medical record (Table 5). Of the three female cases in Livingston, one was classified as a nonsmoker and the other two did not have any smoking history. For a worst-possible-case estimate, investigators assumed that the observed percentage of smokers in the Livingston male cases was the percentage of smokers in the entire Livingston male population. This assumption resulted in the prediction of an increase in the observed pancreatic cancer mortality rate of 7 percent (Figure 4). In fact, the percentage of Livingston male smokers was probably smaller and should have accounted for a smaller increase in the rate.

Figure 3 shows the residential location at the time of death for 11 of the 14 Livingston cases. (Three cases had only a post office box listed on the available records, so their data were not available.) The location of the railroad yard is also shown. Figure 3 suggests a wedge-shaped clustering of cases (nine) around the railroad yard, with a tail of cases (three) east of Highway 89. Of the three cases in the tail east of Highway 89, all three probably had regular occupational contact with the railroad yard. Table 6 shows the age distribution of decedents by 5-year age groups.

The 11 male cases in Livingston included 4 with an occupational history of railroad work (Table 7). The three female cases in Livingston all had an occupational history as housewives.

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Characteristics of Cases in Park County Exclusive of Livingston

Park County exclusive of Livingston had six cases of pancreatic cancer, four were men and two were women. Two of the six cases were histologically confirmed as adenocarcinoma and one histologically interpreted as "probable adenocarcinoma." The latter case and a fourth case for which multiple biopsies did not reveal malignant cells were diagnosed as pancreatic cancer based on the location and pattern of extension of the masses and other features of the clinical presentations. The fifth case had been diagnosed at the University of Minnesota Hospital, Minneapolis, and the details of the diagnostic evaluation were not available. The death certificate for the sixth case, who expired at home and for whom no medical record was located, indicated "hepatic failure" as the immediate cause of death, "hemachromatosis (sic), possible" as the underlying cause that initiated events resulting in death, "ca of pancreas possible" as a condition leading to the immediate cause, and "alcoholism, chronic" under "other significant conditions."

Information on Possible Risk Factors for Cases in Park County Exclusive of Livingston

Of the four male cases in Park County exclusive of Livingston, only one was classified as a smoker according to his medical record; however, no information concerning the number of cigarettes smoked or duration of smoking was given. Two of the three remaining male cases were counted as nonsmokers: one had a history of using chewing tobacco only and the other was reported in the medical record to be a nonsmoker. For the case for which no medical record could be obtained, no smoking history was available. The two female cases were also reported in their medical records to be nonsmokers. The four male cases included a mechanic, a retired accountant and rural mail carrier, and two ranchers, one of whom also had worked as a salesman. The two female rural Park County cases were a school teacher and a school cook. (Table 7).

Comparison of Observed and Expected Case Rates

Table 8 shows the numbers of expected and observed pancreatic cancer (ICD-9-CM code #157) deaths and the associated p-values based on the Poisson distribution for men and women in Livingston, in Park County exclusive of Livingston, and in Park County as a whole for the period 1980 through 1989. The ratio of observed to expected cases for men in Livingston based on the Poisson distribution was 2.34, and was statistically significant ($p < 0.01$). Table 9 shows overall sex-specific, age-adjusted pancreatic cancer mortality rates for the three areas for the period cited. The age-adjusted rate among men in Livingston was about 2.3 times the U.S. rate.

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DISCUSSION

The age-adjusted pancreatic cancer death rates among white men were elevated at a level suggesting a significant increase in Livingston, but not in Park County as a whole, from 1980 through 1989. Since the corresponding rates in Park County exclusive of Livingston were not elevated for men or women, the observed increase in pancreatic cancer mortality was confined to the white male population of Livingston.

Because the Bonferroni correction was used, the appropriate criterion for judging whether each p-value indicated the possibility of a statistically strong association with one of the residential categories was $p < 0.01$ (0.05 divided by 5, the number of digestive-tract cancer sites listed in Table 2). The p-value 0.0092 calculated for white men in Livingston met this more stringent criterion.

Although one of the Livingston decedents had a medical history that questionably supported a diagnosis of pancreatic cancer, the case was included because the death certificate was coded as ICD-CM-9 Code 157, thus meeting the case definition. Furthermore, since the national reference set was based on death certificate codes and contained similar diagnostic problems, it would have been inappropriate to construct the case definition to exclude clinically doubtful cases from the statistical comparisons presented in this report. If a subsequent case-control study is done, a more restrictive case definition may be used, and the accuracy of the diagnosis will be important.

No association has been reported, to date, between pancreatic cancer and the types of exposures (for example, volatile organic compounds, diesel fuel, and asbestos) plausible (on the basis of environmental data and historic information about the railroad yard) for Livingston residents. Previously unobserved associations between a particular disease and an environmental risk factor may be evidenced strongly enough to warrant further investigation. If the evidence accumulated in support of the association meets certain criteria (for example, Hill's modified postulates), it may help to establish a causal relationship between the disease and the risk factor (Kelsey et al, 1986).

The observed percentage of smokers among male cases in Livingston was used to calculate a worst-possible-case estimate of a 7-percent increase in the pancreatic cancer death rate over the U.S. rate (Figure 4). In fact, the percentage of smokers among Livingston males was probably lower than the observed percentage in cases and accounted for a lesser increase in the rate. Thus, in this preliminary investigation, it did not appear to explain the observed elevation in the observed number of Livingston white male deaths. While more detailed information on smoking history obtained in a more rigorous follow-up investigation could better address this question, there is no apparent need for further concern.

The geographic plot of residences in Figure 3 suggested a clustering of cases around the railroad yard. However, a conclusion could not be

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made without also plotting the residences of similar people "at risk" who did not have pancreatic cancer (as might be done in a case-control study).

Table 4 lists the diagnoses of other cancers in addition to pancreatic cancer indicated in the medical records of decedents included in this study. One of the male Livingston residents had a diagnosis of lung cancer 10 years prior to that of pancreatic cancer and a diagnosis of laryngeal cancer 15 years prior to the pancreatic cancer diagnosis. Both cancers can be considered to have been cured because they did not recur or spread within 5 years of the diagnosis. Thus, these earlier diagnoses are not likely to explain the clinical presentation diagnosed as pancreatic cancer. Two other male Livingston residents had diagnoses of prostatic cancer: one 3 years prior to the pancreatic cancer diagnosis and one concurrently. Holleb et al (1991) indicate that prostatic cancer typically spreads to lymph nodes, the bladder, and bone; therefore, metastasis to the pancreas mimicking the presentation of pancreatic cancer would be unlikely in these cases. One male Livingston resident was diagnosed with undifferentiated small-cell carcinoma of the lung concurrent with the diagnosis of pancreatic cancer. Holleb et al (1991) indicate that small cell carcinoma of the lung typically metastasizes to the brain, bone, bone marrow, and lymph nodes, so again metastasis to the pancreas mimicking the presentation of pancreatic cancer would not be likely. Because the remaining decedent, who had diagnoses of two other cancers, was a female Livingston resident, the conclusion of this study would not change, even if the clinical presentation concluded to be pancreatic cancer was, in fact, the result of a different type of cancer.

The prominent group of decedents (36 percent) with occupational histories related to railroad work could have represented a cluster related to occupational exposure, but might also simply have reflected the fact that railroad work was common in Livingston. A comparison with the occupational histories of other people dying of different causes would test the association of occupational factors. The number of decedents who had outdoor occupations might have indicated an etiologic factor, but might also simply have reflected occupational patterns in the area.

Limitations of Study Design

This investigation was based on death certificate and medical record information and, as might be expected, that information was incomplete. The conclusions reached were limited by the lack of important case information, such as the number of years of employment in each occupation, the different street addresses of residences, and the length of residence at each address. Hence, the conclusions are somewhat tentative. Furthermore, given the incomplete environmental data and information on other possible risk factors, even rudimentary speculations about possible causes of the observed increase in white-male, age-adjusted pancreatic cancer death rate for Livingston were not possible.

Overall, 35 percent of the cases of pancreatic cancer were histologically confirmed, and 45 percent of the male Livingston cases were histologically confirmed. These percentages are comparable to the percentage of histologically confirmed cases included in previously published studies of the accuracy of pancreatic cancer diagnoses. In these studies, reported percentages of histologic confirmation were: (1) 30.5 percent (Barklay and Phillips, 1962), (2) 31.5 percent (Mack, 1982), (3) 37.5 percent (Sugultan et al, 1971), and (4) 50.8 percent (Gudjonsson et al, 1978). The comparability to the national data set is reassuring from a methodologic standpoint, but indicates that study power may be reduced.

Potential Sources of Bias

Pancreatic cancer is difficult to diagnose accurately, especially with limited access to sophisticated imaging procedures. Ultimately, the numbers of pancreatic cancer deaths found in this study reflect the combined clinical judgments of a number of practitioners in different specialties. These numerous individual judgments in deciding what clinical tests to use in a diagnostic evaluation, how to interpret the results of those tests, how to read radiologic images, and how to interpret histologic sections created multiple possible sources of bias impossible to evaluate in hindsight. This problem was accentuated in the remote setting of Park County where state-of-the-art diagnostic methods of tertiary care centers were not routinely available. The older methods used are prone to greater subjective variation in interpretation.

Nevertheless, the diagnostic evaluations and medical records were as complete as possible, and the nosologic classifications made appeared to be sound, despite two possible misclassifications. The frequency of misclassification in the comparison data is not known, but such errors would at least partially correct for inclusion of any misclassified cases in this study.

Generating a hypothesis from a data set of multiple cancer-site categories and using the same data for preliminary testing of the hypothesis may increase the probability of chance observation of an apparently significant number of cases; therefore, the Bonferroni method was used to compensate. Use of this correction, which is intended to guard against accepting a false hypothesis, is uncommon because it greatly increases the likelihood of rejecting a true association. Nevertheless, the analysis demonstrated a statistically significant increase in the number of pancreatic cancer deaths among white males in Livingston.

CONCLUSIONS

1. The observed number of Livingston white-male pancreatic cancer deaths from 1980 through 1989 was elevated when compared to the age-adjusted number of deaths expected on the basis of 1980 through 1988 U.S. age and sex specific pancreatic cancer mortality rates and the 1980 census age and sex distribution for Livingston. This difference was statistically significant (p = 0.0092).

2. No significant increase in pancreatic cancer mortality was found in Park County exclusive of Livingston.

3. This investigation was based on a review of death certificates and medical records of a preselected group of cases; it requires corroborative follow up and study before conclusions can be drawn about the risk of pancreatic cancer in Livingston or Park County.
4. There was a suggestion of an occupational clustering, but this suggestion could not be evaluated with the data available.
5. On the basis of this preliminary investigation, smoking does not appear to explain the observed increase in pancreatic cancer mortality for white males in Livingston from 1980 through 1989.

RECOMMENDATIONS

1. A more rigorous epidemiologic investigation should be considered to investigate further the association between pancreatic cancer and environmental factors in Livingston. Such a study should collect and analyze more complete information regarding medical history, residential and occupational history, and other known pancreatic cancer risk factors, such as smoking.
2. Residents of Livingston should be informed of the objectives, methods, findings, and conclusions of this study, including its methodologic limitations.

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ACKNOWLEDGMENTS

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Wynder EL, Hall NE, Polansky M. Epidemiology of coffee and pancreatic cancer. Cancer Res 1983;43:3900.

Table 1--Diagnostic categories of cancer mortality data, 1986-1988, initially provided by the Montana Department of Health and Environmental Sciences for the Agency for Toxic Substances and Disease Registry's review.

Malignant Neoplasms of Lip, Oral Cavity, and Pharynx

Malignant Neoplasms of Digestive Organs and Peritoneum

Malignant Neoplasms of Respiratory and Intrathoracic Organs

Malignant Neoplasms of Bone, Connective Tissue, Skin, and Breast

Malignant Neoplasms of Genitourinary Organs

Malignant Neoplasms of Other and Unspecified Sites (including Brain and Thyroid)

(Information of on total neoplasms in all of these categories was also provided.)

Table 2—Preliminary analysis of cancer mortality, Park County, Montana, for 1986 through 1988.

Category	ICD-9-CM Code	Observed Montana Deaths in Park County (O)	Observed Montana Deaths Not in Park County	Expected Park County Deaths (E)	O:E Ratio
Stomach	151	4	153	2.7	1.48
Colon	153	12	833	14.6	0.82
Rectum, Rectosigmoid	154	3	373	6.5	0.46
Gallbladder	156	2	52	0.9	2.22
Pancreas	157	7	179	3.2	2.19
Total		28	1590	27.9	

Source: (Sperry, 1990)

Table 3--Crude and age-adjusted percentages of smokers in the U.S. population, 1965-1987.

	Male		Female	
Year	Crude	Age-adjusted	Crude	Age-adjusted
1965	51.9	51.6	33.9	34.0
1974	43.1	42.9	32.1	32.5
1979	37.5	37.2	29.9	30.3
1983	35.1	34.7	29.5	29.9
1985	32.6	32.1	27.9	28.2
1987	31.2	31.0	26.5	26.7

Source: (NCHS, 1990)

Table 4--Diagnoses of other cancers, pancreatic cancer cluster investigation, Livingston and Park County, Montana, 1980-1989.

Cancer Site	Years Between Diagnosis and Pancreatic Cancer Diagnosis	Sex	Residence
Lung	10	Male	Livingston
Laryngeal	15		
Metastatic prostatic carcinoma	3	Male	Livingston
"Probable" prostatic carcinoma	Concurrent	Male	Livingston
Undifferentiated small cell lung carcinoma	Concurrent	Male	Livingston
Recurrent skin	Unknown	Female	Livingston
Renal clear cell	Unknown		

Table 5--Smoking history of decedents, pancreatic cancer cluster investigation, Livingston and Park County, Montana, 1980-1989.

	Smokers	Nonsmokers	Unknown
Livingston			
Male	6	4	1
Female	0	1	2
Total	6	5	3
Park County Exclusive of Livingston			
Male	1	3	0
Female	2	0	0
Total	3	3	0
Park County Total			
Male	7	7	1
Female	2	1	2
Total	9	8	3

Table 6--Numbers of decedents by 5-year age groups, pancreatic cancer cluster investigation, Livingston and Park County, Montana, 1980-1989.

Age Group	Livingston Males	Livingston Females	Rural Park County Males	Rural Park County Females
< 39	0	0	0	0
40-44	1	0	0	0
45-49	0	0	0	0
50-54	0	0	0	0
55-59	0	0	1	0
60-64	1	1	1	0
65-69	1	1	0	1
70-74	2	0	1	0
75-79	4	0	1	1
80-84	0	0	0	0
≥85	2	1	0	0

(Numbers of decedents (all zeroes) less than 39 years of age are summed.)

Table 7--Occupations of decedents as ascertained from death certificates and medical records, pancreatic cancer cluster investigation, Livingston and Park County, Montana, 1980-1989.

Livingston Males:		
Four with railroad occupations:	2	Railroad engineers
	1	Railroad boilermaker/welder
	1	Railroad blacksmith and toolmaker
Seven others:	1	Construction foreman/operating engineer
	1	Rancher and prospector
	1	Rancher
	1	Ranch hand
	1	Police officer
	1	Laborer/rancher/automobile repairman
	1	Baker
Rural Park County Males:		
	1	Rancher
	1	Rancher/salesman
	1	Accountant/rural mail carrier
	1	Mechanic
Livingston Females:		
	2	Housewife
	1	Retired housewife
Rural Park County Females:		
	1	School teacher
	1	School cook

Table 8--Strength of association of increased number of pancreatic cancer cases with residential location in Park County, Montana (with 95%-confidence intervals indicated parenthetically), pancreatic cancer cluster investigation, Livingston and Park County, Montana, 1980-1989.

	Observed Deaths (O)	Expected Deaths (E)	O:E Ratio	p-Value
Livingston				
Male	11 (6.20-19.7)	4.7	2.34 (1.32-4.18)	0.0092
Female	3 (1.09-8.77)	5.6	0.54 (0.20-1.58)	0.9150
Total	14 (8.40-23.5)	10.3	1.36 (0.82-2.29)	0.1557
Rural Park County				
Male	4 (1.62-10.2)	2.9	1.40 (0.57-3.58)	0.3218
Female	2 (0.62-7.22)	1.9	1.03 (0.32-3.73)	0.5761
Total	6 (2.81-13.1)	4.8	1.25 (0.59-2.72)	0.3484
Park County Total				
Male	15 (9.15-24.7)	7.6	1.98 (1.21-3.27)	0.0111
Female	5 (2.20-11.7)	6.8	0.74 (0.33-1.72)	0.8046
Total	20 (13.0-30.9)	14.3	1.40 (0.91-2.15)	0.0912

N.B.: The number of deaths expected in one of the geographical units is the sum for all age groups of the product of the U.S. death rates for each 5-year age group per 100,000 population per year times the population of that 5-year age group in the geographical unit, times 10 years, divided by 100,000.

Table 9--Sex-specific, age-adjusted death rates per 100,000 per year, Park County, Montana, for 1980 through 1989.

	Livingston	Rural Park County	Total Park County	United States 1980-88
Male	23.64	14.30	19.99	10.1
Female	6.71	11.43	7.18	9.7
Total	15.01	13.23	14.01	9.9

FIGURE 1: LIVINGSTON RAILROAD YARD PLUME OF TOTAL CHLORINATED ETHYLENE (DICHLOROETHYLENE, TRICHLOROETHYLENE, PERCHLOROETHYLENE) FEBRUARY 1991

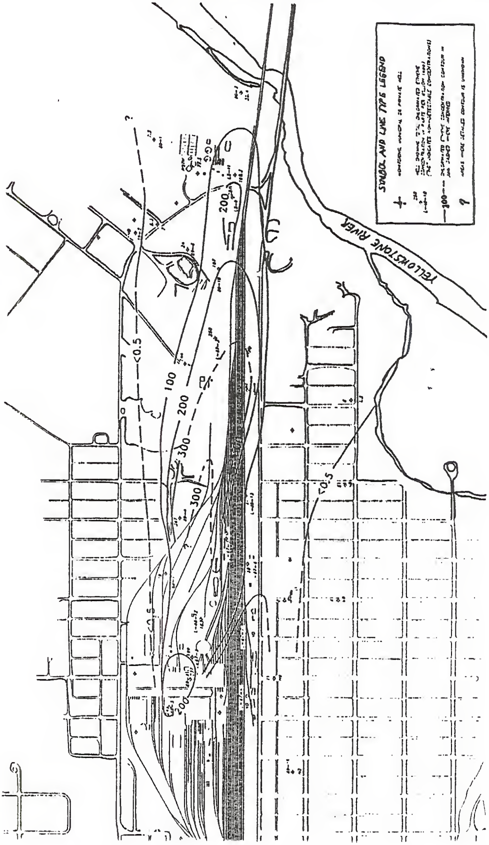

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FIGURE 2: LIVINGSTON RAILROAD YARD PLUME OF DIESEL FUEL FEBRUARY 1991

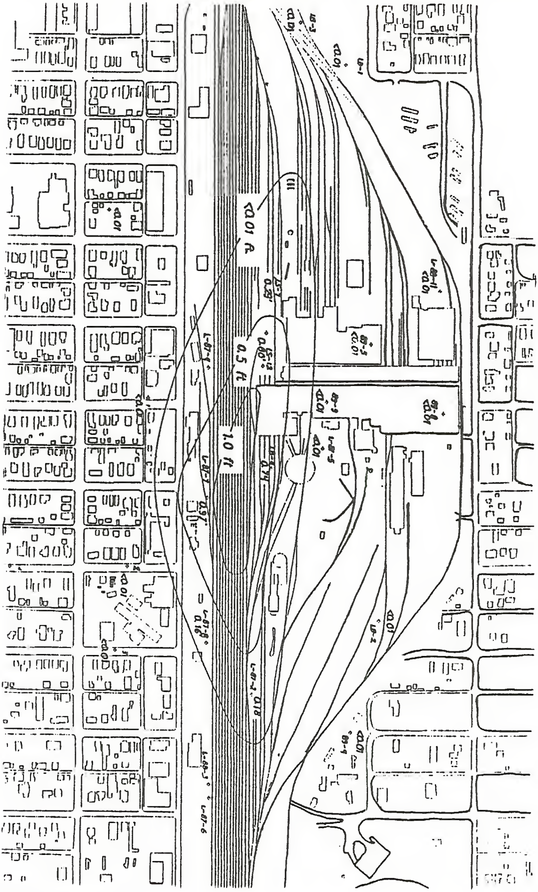

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FIGURE 3--COPYRIGHT PERMISSION PENDING

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Figure 4--Calculation of worst-possible-case estimate of increase in pancreatic cancer mortality for Livingston, Montana.

Let: R = crude U.S. pancreatic cancer mortality rate for males

R′ = crude Livingston pancreatic cancer mortality rate for males

X = male population of Livingston, Montana

Assuming (1) the 1965 crude percentage of smokers in the U.S. male population of 52 percent from Table 3, (2) the threefold increase in pancreatic cancer risk for men who smoke more than 1 1/2 packs of cigarettes per day noted by Wynder et al (1983), and (3) the percentage of 60 percent smokers observed in male cases in this study applied to the Livingston male population as a whole:

$$R = \frac{(.52)(3)X + (.48)X}{X} = 2.04$$

$$R' = \frac{(.60)(3)X + (.40)X}{X} = 2.20$$

Therefore:

$$R'/R = (2.20/2.04) = 1.07$$

Thus, the crude Livingston pancreatic cancer mortality rate for males would be expected to be increased by a factor of 0.07 or 7 percent over the crude U.S. pancreatic cancer mortality rate for males if the percentage of smokers observed among Livingston males in this study was assumed to represent the Livingston male population rather than the crude 1965 percentage of smokers in the male U.S. population. In fact, the percentage of smokers in the Livingston male population was probably lower and hence the increase in pancreatic cancer mortality attributable to smoking was probably less than 7 percent.

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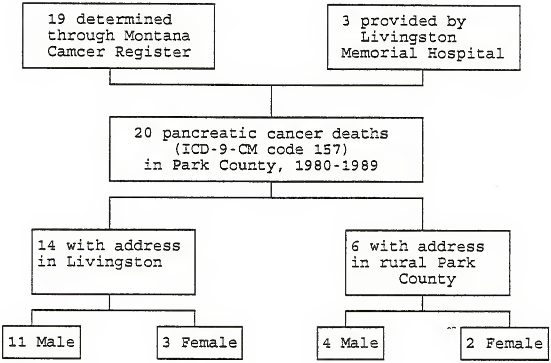
Figure 5 - Origin of cases, place of residence, and distributed by sex.


19 determined through Montana Camcer Register
3 provided by Livingston Memorial Hospital
20 pancreatic cancer deaths (ICD-9-CM code 157) in Park County, 1980-1989
14 with address in Livingston
6 with address in rural Park County
11 Male
3 Female
4 Male
2 Female

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Appendix:
Medical Records Abstraction Form

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DEPARTMENT OF
HEALTH AND ENVIRONMENTAL SCIENCES

STAN STEPHENS, GOVERNOR

FAX #(406) 444-1495

STATE OF MONTANA

OFFICE LOCATION: 836 Front Street
Helena, Montana

MAILING ADDRESS: Cogswell Building
Helena, MT 59620

Medical Record Review

Study/subject number ________

Death Certificate # ____________ Hospital Record # ________________

Other Chart Locater Information ________________________________

Date of Birth ____/____/____ Sex ___ Race __________

Address(es) ________________ ____________________

________________ ____________________

________________ ____________________

Clinical History

Primary Diagnosis: Tissue: ________________ Date ____/____/____

Site: ________ Grade: ______ Stage: ___ Code: __________

At Hospital: ____________ Metastasis? to?________________

(How Dx made, details of diagnostic process, other primaries)

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____

Medical Record Review Study/subject number ________

Remarkable lab or procedure results (with date):

____

____

Who has tissue? ____

____

Secondary Diagnosis:

____

____

____

Smoking, alcohol, dietary history; medications; other risk factors

____

____

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Medical Record Review Study/subject number __________

Usual employment (as much history as is available--place of employment, job title/description, duties, exposures if known)

Spousal occupation(s)—place of employment, job title

Other significant information.

Continue on reverse, if needed. Continued (Y/N)? _____

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